REAL-WORLD EVIDENCE ALLIANCE

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Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Integrating Randomized Controlled Trials for Drug and Biological Products Into Routine Clinical Practice; Draft Guidance for Industry; Availability (Docket No. FDA-2024-D-2052)

To the Food and Drug Administration:

The RWE Alliance appreciates the opportunity to comment on the draft guidance titled "Integrating Randomized Controlled Trials for Drug and Biological Products Into Routine Clinical Practice" ("Draft Guidance").[1] We are a coalition of real-world data ("RWD") and analytics organizations with a common interest in harnessing the power of real-world evidence ("RWE") to inform regulatory decision making to improve the lives of patients. Our members have deep knowledge and experience working with healthcare data across disease areas and patient populations, and we aim to bring these collective insights to bear in support of RWE policies.[2]

The RWE Alliance envisions a future in which data from electronic health records, administrative claims and billing records, product and disease registries, personal devices, wearables, and health applications will be used to generate evidence to support regulatory decision making related to medical product safety and effectiveness. To achieve these goals, the RWE Alliance advocates for policies that will (1) advance FDA's RWE Framework, (2) encourage the use of RWE to better understand treatment effects in underrepresented populations, (3) enhance opportunities for RWE organizations to consult with FDA, (4) increase communication on the generation and use of RWE, and (5) recognize the unique aspects of and opportunities for RWD/E.[3]

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[1] 89 Fed. Reg. 76482 (Sept. 18, 2024).

[2] For information about our members, please see our website, https://rwealliance.org/who-we-are/.

[3] Additional information about what we believe is available on our website, https://rwealliance.org/what-we-believe/.

We appreciate FDA releasing this Draft Guidance to support the integration of research into routine clinical practice. Section I of this letter provides general comments on the Draft Guidance, and Section II provides specific comments on topics addressed in the Draft Guidance.

I. General Comments on the Draft Guidance

We recommend that FDA provide more specific guidance regarding the collection of data elements for randomized controlled trials ("RCTs") in routine clinical practice. We agree with the Draft Guidance that data elements for routine services will be found in the patient file or electronic medical record (e.g., blood pressure readings). We also appreciate FDA's recognition that there may be variation in the frequency of clinical or laboratory measurements in the clinical setting. We believe study designers could benefit from more detailed FDA recommendations on appropriate methods to address imbalances in the frequency of data collection across patients or sites. Examples of methods that FDA considers sufficient to ensure that measurement occurs at a "reasonably consistent frequency," as the Draft Guidance recommends on lines 392–94, would be particularly helpful. Sponsors also would benefit from additional discussion on the staff responsibilities for collecting and inputting those data. Understanding these details and accounting for potential sources of variation will aid sponsors in site selection, protocol design, and data analysis.

II. Comments on Specific Sections of the Draft Guidance

The following subsections provide our comments on specific sections of the Draft Guidance. For ease of reference, the headings for each subsection correspond to the headings used in the Draft Guidance.

A. Streamlining RCTs To Align With Clinical Practice

In lines 236–39, the Draft Guidance discusses the concept of a "hybrid approach" of collecting study data that are not routinely collected by local healthcare providers ("HCPs"). The Draft Guidance states, "It may not be feasible for all trial procedures to be performed by local HCPs during routine care visits, and in these situations, sponsors can consider a hybrid approach, combining data contributed by local HCPs with study-specific procedures performed by trial personnel." We agree that RCT-specific data that are not routinely collected would sometimes be needed to measure endpoints for effectiveness studies or for more complex safety measures. To advance the field, we encourage FDA to disseminate examples of hybrid approaches for RCT data collection that it deems to be appropriate—including examples that include the collection of validated clinical outcome assessments ("COAs"), decentralized data collection techniques, remote patient monitoring, and/or remote study monitoring approaches.

B. Study Endpoints

We agree with the Draft Guidance that many RCTs rely on COAs to assess patients' functional status or symptoms. The use of COAs in routine clinical practice is evolving. Increasingly adaptable technologies facilitate a wider collection of both clinician-

reported and patient-reported data for community providers and researchers alike. We suggest that FDA recognize this trend and discuss how the growing use of patient-reported outcome measures, digital diagnostics, and remote monitoring systems present opportunities for more pragmatic data collection. We encourage FDA and stakeholders to encourage adoption of such tools and thereby enhance the availability of data from local HCPs for a particular RCT, as well as harness such tools to collect additional research-specific data elements in hybrid approaches.

The RWE Alliance appreciates the Agency's commitment to advancing the use of RWD and RWE in regulatory decision making. Thank you for considering these comments, and please let us know if you have any questions. We welcome the opportunity to discuss further.

Best regards,

The RWE Alliance